UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/081,522	05/19/1998	PETER BROOKS	TSRI419OCONI	1607

7590 05/29/2002

THE SCRIPPS RESEARCH INSTITUTE
10550 NORTH TORREY PINES ROAD
MAIL DROP TPC 8
LA JOLLA, CA 92037

EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	13

DATE MAILED: 05/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/081,522	Applicant(s) BROOKS ET AL.
	Examiner GAMBEL	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 3/12/01; 10/15/01

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 171-~~188, 205~~-286

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 189-204

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 171-188, 205-286

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☑ The drawing(s) filed on 12/3/01 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

#23

DETAILED ACTION

1. Applicant's provisional election with traverse the species (B) breast tumor growth, if no generic claims finally held to be allowable, in Paper No. 22, filed 3/12/02, is acknowledged.

Applicant traverse the Restriction Requirement on the grounds that the multiplicity of the species does not require an extensive and burdensome search.

However, this is an election of species not Groups and has been treated as an election of species.

Applicant is reminded of the following with respect to the election of species.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Given that applicant does not admit or provide evidence the species are obvious variants, the species requirement is maintained for the reasons of record.

Claims 171-188, 205, -221, 222-239, 40-251, 252-269 and 270-286, as they read methods of inhibiting breast cancer of treatment with $\alpha_v\beta_3$-specific antibodies / LM609-specific antibodies are under consideration in the instant application.

Claims 189-204 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected species.

Claims 1-170 have been canceled previously.

2. Applicant's arguments and newly added claims, filed10/15/01 (Paper No. 17), are acknowledged.

Given the elected invention methods of inhibiting breast cancer of treatment with $\alpha_v\beta_3$-specific antibodies / LM609-specific antibodies, New Grounds of Rejection have been set forth herein.

3. Formal drawings, filed 12/3/01 (Paper No. 19) comply with 37 CFR 1.84.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined *under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).*

5. The previous rejections under 35 U.S.C. § 102(a) as being anticipated by Kim (WO 93/20229), under 35 U.S.C. § 102(b) as being anticipated by Cheresh (WO 89/05155; 1449) and under 35 U.S.C. § 103(a) as being unpatentable over Kim (WO 93/20229; 1449) AND/OR Cheresh (WO 89/05155; 1449) in view of Nicosia et al. (Am. J. Pathol. 138: 829 - 833, 1991; 1449), Nip et al. (J. Clin. Invest. 90: 1406-1413, 1992; 1449) , Folkman et al. (Seminars in Cancer Biology 3: 89-96, 1992; 1449) and art known procedures to treating cancers of interest at the time the invention was made have been withdrawn as they read on the elected invention of methods of treating breast cancer with αvβ3-specific antibodies.

6.Claims 171-188, 205, -221, 222-239, 40-251, 252-269 and 270-286 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kim (WO 93/20229; 1449) AND/OR Cheresh (WO 89/05155; 1449) in view of Nicosia et al. (Am. J. Pathol. 138: 829 - 833, 1991; 1449), Nip et al. (J. Clin. Invest. 90: 1406-1413, 1992; 1449) , Folkman et al. (Seminars in Cancer Biology 3: 89-96, 1992; 1449), Pignatelli et al. (Hum Pathol 23:1159-1166 (1992) and conventional or art known procedures to treating cancers of interest at the time the invention was made, as taught by the references set forth herein or acknowledged on pages 13-23 of the instant specification.

Kim teaches neutralizing antibodies, including humanized and antibody fragments, that bind αvβ3, including the LM609 antibody, that inhibit binding tumor cells with vitronectin, fibrinogen and von Willebrand factor in vivo, in order to inhibit tumor growth and metastasis because tumor growth depends on cell attachment, (see entire document, including Background of the Invention, Summary of the Invention, and Detailed Description of the Invention; also, see page 6, paragraph 2; page 9, paragraph 2)

Kim also teaches modes of administration and doses of therapeutic antibody alone or in combination with other agents that are effective for the same clinical objective, depending on the type of the disease, the severity and course of the disease in the individual at the discretion of the practitioner (pages 9-10); wherein said modes of administration and doses are encompassed by the claimed methods

Although the Kim reference does not state an "angiogenesis-inhibiting amount" per se; the tumor-inhibiting amount taught by the reference would intrinsically or expectedly encompass the "angiogenesis-inhibiting amount" encompassed by the claimed methods.

Cheresh teach antibodies that bind the RGD-directed adhesion receptor, including the LM609 antibody specificity to inhibit binding of this receptor with vitronectin, fibrinogen and von Willebrand factor in vivo, in order to inhibit tumor growth because tumor growth depends on cell attachment (see entire document, including Therapeutic Methods and Compositions on pages 20-23) .

Here, Cheresh also teach modes of administration and doses of therapeutic antibody compositions to meet the needs of the individual and dependent upon the judgement of the practitioner; wherein said modes of administration and doses are encompassed by the claimed methods.

Although the Cheresh reference does not teach the "αvβ3" specificity per se; the LM609 intrinsically binds the αvβ3 specificity encompassed by the claimed methods.

Although the Cheresh reference does not state an "angiogenesis-inhibiting amount" per se; the tumor-inhibiting amount taught by the reference would inherently encompass the "angiogenesis-inhibiting amount" encompassed by the claimed methods.

The primary references do not disclose targeting breast cancer with αvβ3-specific or LM609-specific antibodies per se.

Pignatelli et al. identified changes with with αv integrins on breast epithelia during malignant transformation and identified the integrin with αvβ3 in a high percentage of invasive lobular carcinomas in breast cancer patients (see entire document, including Abstract). Pignatelli et al. Also state that overexpression of integrin molecules mediating cell migration such as αvβ3 may allow the tumor cells to invade the adjacent tissued and vascular channels and contribute to metastasis as shown in malignant melanomas. Pignatelli et al. Further states that the detection of αv chain in poorly differentiated carcinomas is highly suggestive of a similar role played by the vitronectin receptor in the progression of invasive breast carcinomas and that the finding that αvβ3 is expressed in more ILCs than IDCs has some significance in the differing biologic behavior of these cell types (see page 1164, column 2, lines 25-33).

Although the primary references do not teach certain modes of administration such as peristaltic administration and following surgery to remove a solid tumor per se ; it would have been readily apparent to one of ordinary skill in the art at the time the invention was made to provide the αvβ3/ RGD-specific inhibitors, including the LM609 to meet the needs of the patient, as these claimed limitations were conventional at the time the invention was made and the prior art teaches treating patients with αvβ3/ RGD-specific inhibitors, including the LM609 in conjunction with conventional therapy.

In addition to the conventional or art known procedures, including dosages, modes of administration and regimens in order to meet the needs of the patients and to inhibit tumor growth to treating cancers of interest at the time the invention was made, as taught by the references set forth herein (e.g. pages 9-10 of Kim) or acknowledged on pages 13-23 of the instant specification.

It is noted that Kim teaches the art known use of recombinant antibodies and antibody fragments, while Cheresh does not. Given the teachings of various antibody αvβ3 antibody antagonists; it would have been obvious to the ordinary artisan to employ various antibody inhibitors, including the conventional antibody fragments, encompassed by the claimed invention, provided they inhibited αvβ3/ RGD-specific interaction

In addition to Cheresh and Kim; Nip et al teach the role of αvβ3-RGD mediated interactions in the metastasis with cancers, including melanoma (see entire document) and the ability to block such interactions via αvβ3/ RGD-specific inhibitors, including the LM609 antibody (see entire document, including the Abstract, Introduction and Discussion).

Nicosia et al. teach inhibiting angiogenesis by a RGD inhibitor (see entire document, including the Abstract).

Again while the primary references do not state an "angiogenesis-inhibiting amount" per se; the tumor-inhibiting amount taught by the reference would have the expected properties of an "angiogenesis-inhibiting amount" encompassed by the claimed methods; given the combined teachings of inhibiting tumor growth and metastasis with αvβ3/ RGD-specific inhibitors, including the LM609 and RGD inhibitors inhibit angiogenesis.

Also, it was known at the time the invention was made that angiogenesis was necessary but not sufficient for expansion of tumor population, as taught by Folkman et al. (See entire document, particularly Rationale of anti-angiogenic therapy on page 89).

Folkman et al. Also teach that angiogenesis inhibitors may be administered to cancer patients in conjunction with convention chemotherapy for the control of metastatic disease such as prostate, breast or colon cancer (see page 94, column 1, paragraph 3).

Given the teachings of various antibody αvβ3 antibody antagonists; it would have been obvious to the ordinary artisan to employ various antibody inhibitors, including the conventional antibody fragments (e.g.; claims 23, 36, 78, 163) encompassed by the claimed invention, provided they inhibited αvβ3/ RGD-specific interaction

One of ordinary skill in the art at the time the invention was made would have been motivated to select αvβ3/ RGD-specific inhibitors such as αvβ3-specific antibodies such as the LM609 specificity to inhibit tumor growth and metastasis in combination with conventional therapy to treat cancer. Providing αvβ3-specific antibodies such as the LM609 in "angiogenesis-inhibiting amounts" encompassed by the claimed methods would have been expected; given the prior art teaching of inhibiting tumor growth and metastasis. Also, given the metastatic behavior of various tumors, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply such therapeutic intervention to target various tumor types, including those from bladder, breast, colon or lung.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
May 28, 2002